

IN THE CLAIMS

Please cancel claim 2 and replace claims 1, 3-19, 22, and 24-26 with the following amended claims. A marked-up version of the amendment, indicating changes in the claims, is attached hereto as Appendix A.

1. (Twice Amended) A polyamide molecule that specifically binds to base pairs in the minor groove of a DNA molecule, said polyamide molecule comprising:

one or more amino acids comprising a moiety selected from the group consisting of N-methylpyrrole, 3-hydroxy-N-methylpyrrole, and N-methylimidazole, wherein one or more of said amino acid(s) are not α -amino acids; and

a positive patch consisting of a rigid group adjacent to a positively charged group, said rigid group comprising a first and a second amino acid; said first amino acid being selected from the group consisting of arginine, proline, lysine, and hydroxyproline; and said second amino acid being selected from the group consisting of proline, glycine, serine, threonine, leucine, isoleucine, valine, alanine, and hydroxyproline.

3. (Amended) The polyamide of claim 2 wherein said first amino acid is arginine and said second amino acid is proline.

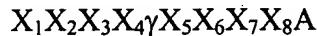
4. (Amended) The polyamide of claim 1 wherein the positively charged group comprises a synthetic or naturally occurring amino acid having a net positive charge.

5. (Amended) The polyamide of claim 1 wherein said positively charged group is selected from the group consisting of a primary amino group, secondary amino group, tertiary amino group, quartenary amino group, guanidinium group, and an amidinium group.

6. (Twice amended) The polyamide of claim 1 wherein said positively charged group is selected from the group consisting of arginine, lysine, and histidine.

7. (Amended) The polyamide of claim 1 wherein said positively charged group is arginine.
8. (Amended) The polyamide of claim 1 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.
9. (Amended) The polyamide of claim 1 wherein the polyamide has three or four carboxamide binding pairs.
10. (Amended) The polyamide of claim 1 wherein the polyamide comprises an (R)-2,4-diaminobutyric acid hairpin turn that facilitates specific binding to base pairs in the minor groove of a DNA molecule.
11. (Amended) The polyamide of claim 10 wherein the R-2-amino group is derivatized to form an acid amide.
12. (Twice Amended) The polyamide of claim 1 having the formula:
$$X_1 X_2 X_3 \gamma X_4 X_5 X_6 A$$
wherein γ is $-\text{NH-CH}_2\text{-CH}_2\text{-CH}_2\text{-CONH-}$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;
 X_1/X_6 , X_2/X_5 , and X_3/X_4 represent three carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of 3-hydroxy-N-methylpyrrole/N-methylpyrrole (Hp/Py), N-methylpyrrole/3-hydroxy-N-methylpyrrole (Py/Hp), N-methylpyrrole/N-methylimidazole (Py/Im), N-methylimidazole/N-methylimidazole (Im/Py), and N-methylpyrrole/N-methylpyrrole (Py/Py) to correspond to the DNA base pair in the minor groove to be bound; and
A represents said positive patch consisting of a rigid group adjacent to a positively charged group.
13. (Amended) The polyamide of claim 12 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

14. (Twice amended) The polyamide of claim 1 having the formula:



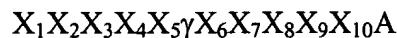
wherein γ is $-NH-CH_2-CH_2-CH_2-CONH-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_8 , X_2/X_7 , X_3/X_6 , and X_4/X_5 represent four carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of Hp/Py, Py/Hp, Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound; and

A represents said positive patch consisting of a rigid group adjacent to a positively charged group.

15. (Amended) The A polyamide of claim 14 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

16. (Twice amended) The polyamide of claim 1 having the formula:



wherein γ is $-NH-CH_2-CH_2-CH_2-CONH-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_{10} , X_2/X_9 , X_3/X_8 , X_4/X_7 , and X_5/X_6 represent five carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of Hp/Py, Py/Hp, Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound; and

A represents said positive patch consisting of a rigid group adjacent to a positively charged group.

17. (Amended) The polyamide of claim 16 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

18. (Twice amended) The polyamide of claim 1 having the formula:



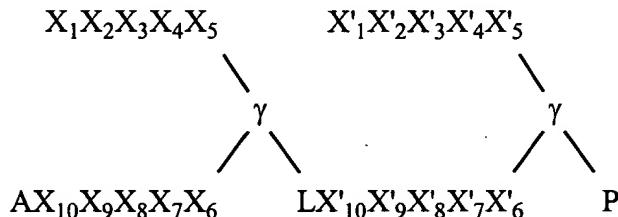
wherein γ is $-NH-CH_2-CH_2-CH_2-CONH-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_{12} , X_2/X_{11} , X_3/X_{10} , X_4/X_9 , X_5/X_8 , and X_6/X_7 represent six carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of H_p/P_y , P_y/H_p , P_y/I_m , I_m/P_y , and P_y/P_y to correspond to the DNA base pair in the minor groove to be bound; and

A represents said positive patch consisting of a rigid group adjacent to a positively charged group.

19. (Amended) The polyamide of claim 18 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

22. (Twice Amended) A tandem-linked polyamide having the formula:



wherein γ is $-NH-CH_2-CH_2-CH_2-CONH-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_{10} , X_2/X_9 , X_3/X_8 , X_4/X_7 , X_5/X_6 , X'_1/X'_{10} , X'_2/X'_9 , X'_3/X'_8 , X'_4/X'_7 , and X'_5/X'_6 represent carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of H_p/P_y , P_y/H_p , P_y/I_m , I_m/P_y , and P_y/P_y to correspond to the DNA base pair in the minor groove to be bound;

L represents an amino acid linking group selected from the group consisting of β -alanine and 5-aminovaleric acid (δ);

P represents a polyamide selected from the group consisting of $X_1X_2X_3\gamma X_4X_5X_6$, $X_1X_2X_3X_4\gamma X_5X_6X_7X_8$, $X_1X_2X_3X_4X_5\gamma X_6X_7X_8X_9X_{10}$, and $X_1X_2X_3X_4X_5X_6\gamma X_7X_8X_9X_{10}X_{11}X_{12}$, where X_1-X_{12} are independently selected from the group consisting of β -alanine, pyrrole, hydroxypyrrrole and imidazole; and

A represents a positive patch consisting of a rigid group adjacent to a positively charged group.

24. (Amended) The polyamide of claim 1 selected the group consisting of:

ImPyPyPy- γ -PyPyPyPy- β -RPR;
ImImPyPy- γ -ImPyPyPy- β -RPR;
ImPyPyPy- γ -PyPyPyPy- β -RPRRRR;
ImImPyPy- γ -ImPyPyPy- β -RPRRRR;
ImPyPyPy- γ -PyPyPyPy- β -R;
ImPyPyPy- γ -PyPyPyPy- β -RP;
ImPyPyPy- γ -PyPyPyPy- β -RGR;
ImPyPyPy- γ -PyPyPyPy- β -R^DPR;
ImPyPyPy- γ -PyPyPyPy- β -APR;
ImPyPyPy- γ -PyPyPyPy- β -KPR;
ImPyPyPy- γ -PyPyPyPy- β -RPK;
ImPyPyPy- γ -PyPyPyPy- β -C7-RPR; and

the pharmaceutically acceptable salts thereof.

25. (Amended) A method of inhibiting gene expression comprising contacting a regulatory sequence of a gene with the polyamide of claim 1.

26. (Amended) A method of inhibiting gene expression comprising contacting a DNA molecule with the polyamide of claim 1 whereby the DNA molecule is conformationally constrained.